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Homocysteine augments BK channel activity and decreases exocytosis of secretory granules in rat GH3 cells

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Abstract

© 2016 Federation of European Biochemical SocietiesIn this study, we investigated the effects of L-homocysteine (Hcy) on maxi calcium-activated potassium (BK) channels and on exocytosis of secretory granules in GH3 rat pituitary-derived cells. A major finding of our study indicates that short-term application of Hcy increased the open probability of oxidized BK channels in inside-out recordings. Whole-cell recordings show that extracellular Hcy also augmented BK currents during long-term application. Furthermore, Hcy decreased the exocytosis of secretory granules. This decrease was partially prevented by the BK channel inhibitor paxilline and fully prevented by N-acetylcysteine, a reactive oxygen species scavenger. Taken together, our data show that elevation of cellular Hcy level induces oxidative stress, increases BK channel activity, and decreases exocytosis of secretory granules. These findings may provide insight into some of the developmental impairments and neurotoxicity associated with Hyperhomocysteinemia (HHcy), a disease arising due to abnormally elevated levels of Hcy in the plasma.

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Keywords

BK channels, exocytosis, homocysteine, oxidative stress